INOCULATION AGAINST MALARIA

BY

DR. PHILALETHES KUHN

STAFF SURGEON TO THE IMPERIAL TROOPS OF THE SOUTH WEST AFRICA PROTECTORATE

TRANSLATED BY

H. A. NESBITT, M.A.

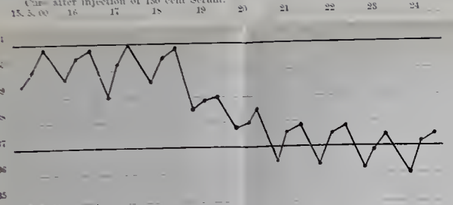
WITH A TABLE OF CURVES

LONDON

H. K. LEWIS, 136 GOWER STREET, W.C.

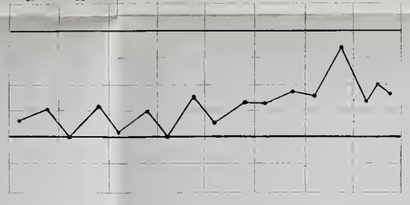
1902

Curve 1.
Horse. Natural Horse-sickness.
Cure after injection of 130 ccm Serum.

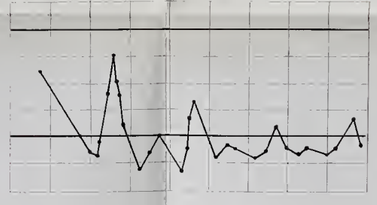


Curve 2.
Horse. Natural Horse-sickness.
Cure after injection of 100 ccm Serum.

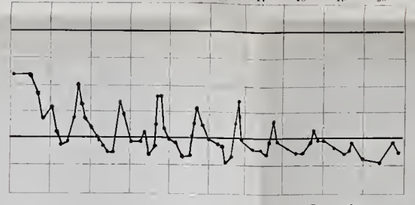
Curve 3.
Horse. Inoculation with ·05 ccm disease blood March 18 th 1899.
Died March 27 th 1899.



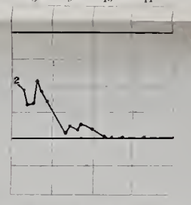
Curve 4.
German, age 35. Tertian. Suffered from Malaria in May 1899 and since Nov. 1900. Inoculation of 2 ccm Serum. Jan. 18 th 1901.



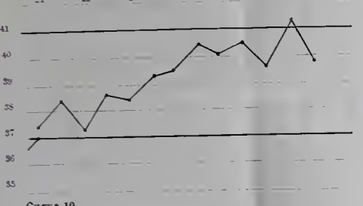
Curve 5
German Woman, age 20. Has Malaria for the first time. Quotidian.
Injection of 2 ccm. Nov. 14 1901.



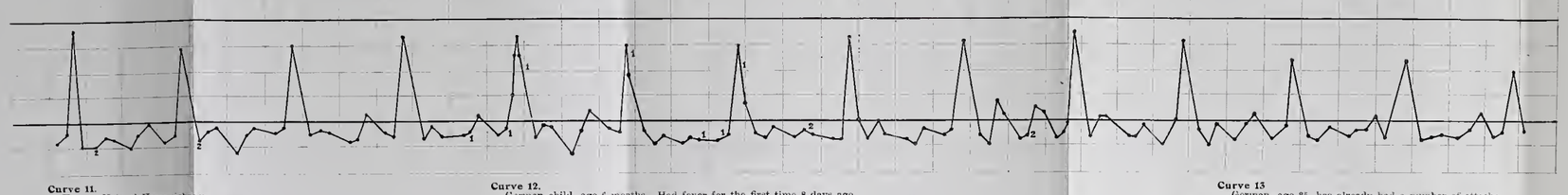
Curve 6.
German, age 30. Suffered from Malaria every 4 or 5 months since the rainy season of 1899. Inoculation of 2 ccm Nov. 8 th 1901. Tertian.



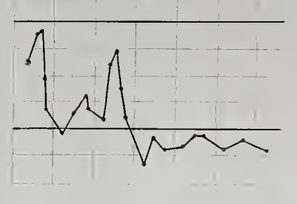
Curve 7.
Horse. Sickness commenced by inoculation of ·05 ccm disease blood March 18 th 1899 died March 21 st 1899.



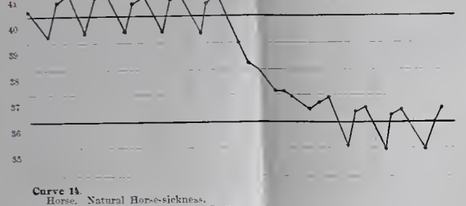
Curve 8.
German, age 28. Has had a few attacks of fever. Quartan Inoculation on different days.



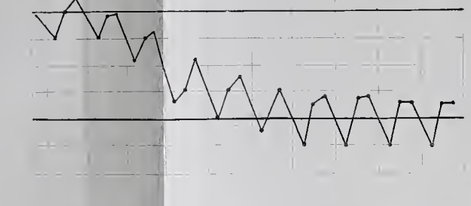
Curve 9.
German, age 40, has already had much fever. Inoculation of 2 ccm Serum Dec. 17 th 1900. Tertian.



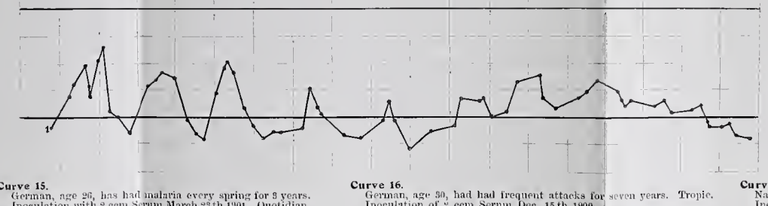
Curve 10.
Horse. Natural Horse-sickness.
Cure after injection of 110 ccm Serum.



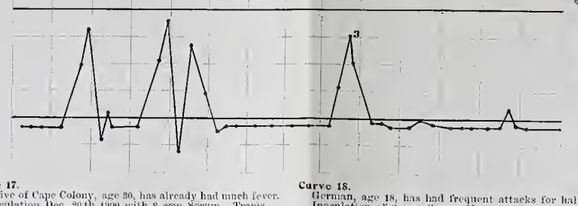
Curve 11.
Horse. Natural Horse-sickness.
Cure after injection of 100 ccm Serum.

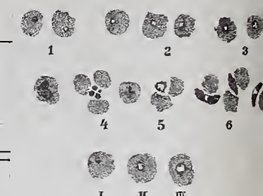


Curve 12.
German child, age 6 months. Had fever for the first time 8 days ago.
Tropic. Inoculation of 1 ccm Serum May 29 th 1900.

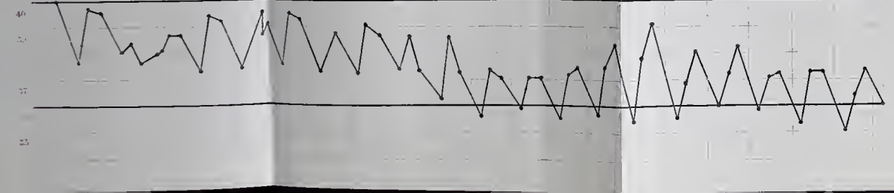


Curve 13
German, age 35, has already had a number of attacks.
Inoculation Nov. 11 th 1901 with 3 ccm Serum. Tertian.

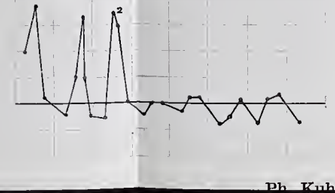




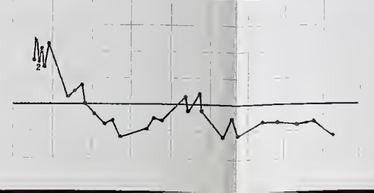
Curve 14.
Horse. Natural Horse-sickness.
Cure after injection of 100 ccm Serum.



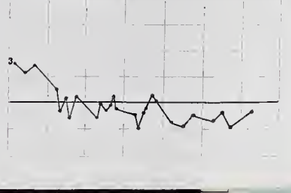
Curve 15.
German, age 26, has had malaria every spring for 3 years.
Inoculation with 2 ccm Serum March 23 th 1901. Quotidian.



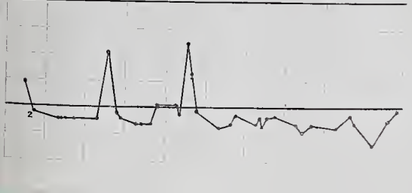
Curve 16.
German, age 50, had had frequent attacks for seven years. Tropic.
Inoculation of 2 ccm Serum Dec. 15 th 1900.



Curve 17.
Native of Cape Colony, age 30, has already had much fever.
Inoculation Dec. 20 th 1900 with 2 ccm Serum. Tropic.



Curve 18.
German, age 18, has had frequent attacks for half a year past.
Inoculation of 2 ccm Serum Nov. 10 th 1900. Tertian.



Ph. Kuhn

Inoculation against Malaria

by

Dr. Philalethes Kuhn.

Staff Surgeon to the Imperial Troops of the South West Africa Protectorate

With a Table of Curves.

GRATEFULLY DEDICATED

TO

COLONEL LEUTWEIN

GOVERNOR OF GERMAN SOUTH WEST AFRICA

BY

THE AUTHOR.

Inoculation for Malaria.

I propose in the following pages to give a short description of observations I have made and conclusions I have formed during a residence of five years in German South West Africa in regard to a serum for inoculation against Malaria, and to give an account of my experience in the use of the serum up to the present time.

A. Horse Sickness.

The study of this malady was first taken in hand by Joshua Nunn, an English veterinary surgeon, in 1887. Then Edington of Grahamstown brought out a large number of valuable publications on the subject. The question has also been specially dealt with by Dr. Sander, a navy surgeon, by a farrier named Rickmann and by a veterinary surgeon of Prætoria named Theiler.

Of the researches made by me in conjunction with First Lieutenant Otto Eggers I will only mention those which are necessary for the actual subject matter of this pamphlet. A more detailed account of the disease and of the labours of earlier enquirers is reserved for a special publication.

Horse-sickness is an acutely infectious disease affecting horses, mules and hinnies in South Africa. In South West Africa it prevails in those localities where Malaria exists. The places where the sickness is not met with or occurs but seldom and in isolated cases are, curiously enough, called "sickness places". Animals are brought to these places at the season when the Sickness prevails. This season lasts about five months and coincides with the mosquito season, and with the time when fresh infections of malaria occur. It appears that the mosquitoes carry the infection.

The Sickness is not directly communicated from one horse to another. Animals may come into close contact with the corpses of animals that have died of it, they may stand in the same stall, eat and drink from the same pail as infected horses without catching it.

In order to protect horses in an infected district during the rainy season, they must be brought into stables or *kraals*.*) where they must stand close together. The mosquitoes avoid the pungent vapour that rises, as they would avoid tobacco smoke. Some stables afford complete protection, while others are as bad as the open air. A spacious stable holding few horses, and with large openings for

Horse-Sickness. Ill. 1.

the free passage of air, retains little smell and does not deter the mosquitoes. In the same way a large kraal with not many horses is no protection at all. But a lowlying kraal, crowded with cattle and horses and redolent of dung, may afford very great protection. The horses must be brought in before sunset and not let out until after sunrise, as the mosquitoes begin to buzz early in the evening and do not begin to settle till the morning.

*) Kraal is the South African name for an enclosure for cattle.

Dew, which used to be generally considered as the cause of the Sickness, is quite innocent. It only occasionally coincides with the plague of mosquitoes.

As the mosquitoes in some instances buzz even in the daytime, when they are disturbed in the high grass, the bushes or the fields of maize where they love to settle during the day,

Horse-Sickness. Ill. 2.

there is always a certain danger that the horses may be infected while pasturing. This explains the cases in which farmers have lost their horses in spite of all their care, in spite of their placing them in confined stables and only letting them out for a few hours in the day.

In the districts of Cape Colony, the Orange Colony and Natal, the Sickness makes its appearance only in certain years, but it then takes the form of a violent epidemic. Since 1763, the time of the first recorded outbreak, seven great epidemics have

been registered. The last, during the Rainy Season of 1891/92, carried off 14,128 animals in Cape Colony, in 1854/55 70000 horses and asses died, valued at £ 525,000 (Official Handbook of the Cape of Good Hope, 1893). Further north, in the Transvaal, Bechuanaland, German South West Africa as far as the Portuguese possessions and the regions of Central Africa the disease appears every year and in about the same intensity. It becomes more and more violent as the land lies more to the north. In these regions plentiful use is made of the "Sickness Places", where they exist.

After infection several days pass before the disease shows itself. With natural infection it takes seven, eight or nine days. The temperature of the body is frequently 104° to 106° F. on the day when it appears. Careful observation of the animals shews that commencement of the fever is accompanied by langnor, muscular weakness, and wandering. The exposed mucous membranes become red, the breathing is accelerated, and there is often a dry cough.

Ordinarily however the disease is not noticed until the animal stands still from great faintness, refuses his food and can only be driven forward with difficulty. It is then found that the skin of the head, particularly the face, that of the passage of the throat, and frequently that of the neck and breast, or even the belly and legs is swollen. The skin protrudes from the sockets of the eyes and the passage of the throat. The eyes water.

In the accompanying illustration (Ill. 1.) we see the head of a horse distinctly swollen, while the skin protrudes like a ball at the sockets of the eyes. The horse however is still able to take lively observation, as is evinced by the eyes and the position of the ears.

A few hours later (Ill. 2) the animal is completely swollen up. We see by the attitude of the ears that he is without consciousness of the outer world. He is still able to stand. Death followed a few minutes after the second photograph was taken.

The disease is often accompanied by inflammation of the mouth, there is a flow of saliva and a difficulty in swallowing, the animal is continually trying to chew. The tongue gets bigger and bigger, and finally protrudes between the teeth and becomes bluish.

From the time when the symptoms of the Sickness have become distinctly evident it lasts but a few hours. Then the breathing becomes laboured, the coughing more violent, yellow mucous comes from the nostrils and is brought up by coughing. The sides palpitate, the flow from the nose gets frothy. In

consequence of the entrance of water into the lungs, death takes place with convulsions. The approach of death is marked by the appearance of sweat, particularly on the belly and breast, and by a marked fall of temperature.

From the moment when the man in charge first notices that the horse is ill, seldom more than half a day elapses before its death. It frequently happens that a horse is ridden without any sign of its being ill, and that directly afterwards it falls sick and dies.

The South African farmers distinguish between two forms of the disease, which they call Dikkopziekte and Dünnperdziekte. In the former the head is much swollen (see the two illustrations), in the latter the swelling is slight. The former is considered to be less severe. The reason for this indeed is that the second form has to do with cases in which the beast becomes weak so quickly that death follows before extensive swellings have had time to show themselves. In reality there is no difference.

When an animal recovers from natural horse-sickness it remains subject to high fever for one or two weeks, but there is no effusion of water in the lungs.

The swelling and the cough gradually disappear, but the evening temperature remains high for some time longer. The morning temperatures are either already normal or only slightly above the normal.

In most cases there is a relapse only lasting for a few days, from nine to ten days after the maximum point of the fever. During this time the horses are dull and languid, but few of the symptoms of the disease are discernible. Relapses may take place repeatedly.

It is not until six weeks after the time when it began to sicken that an animal can be looked upon as cured, as before that time exertion may bring on a return of the fever and other symptoms, or even death. Gradually the animal arrives at a complete state of immunity. It is "salted".

A 'salted' horse is looked upon in South Africa as lazy, the skin of the neck often remains thick and wanting in elasticity. Frequently a chronic cough remains.

The most striking thing about the body after death is for the most part the flow of yellowish frothy fluid from the nostrils, which often forms a regular puddle. Sometimes there is only a yellowish white foam hanging from the nostrils.

The skin of the head, throat, neck and breast is dropsical and swollen. In the meshes of the subcutaneous areolar tissue there

is a clear light yellow serum. The lymphatic glands in the neighbourhood of the swellings are enlarged.

The whole of the mucous membrane is for the most part inflamed and red. The mucous membrane lining the cavity of the mouth is often of a bluish red and thickened. The tongue is at times enlarged and misshapen. Even the mucous membrane of the air passages is often swollen, as is also the conjunctiva, which becomes red. The fibrous tissue which surrounds the trachea and its branches and helps to fill the space of the mediastine is saturated with a briny liquid. The saturation observed in the fibrous tissue may also be found in all the organs, particularly the kidneys.

The lungs are dropsical and swollen. On incision a quantity of yellowish fluid and froth exudes which is increased by pressing upon the bronchial tubes.

The trachea and its branches are filled with a yellowish frothy liquid.

The pleura is inflamed and swollen, frequently having deposits of salt upon it. In the cavity of the chest there are often two gallons and more of water, for the most part light yellow and clear, but sometimes with a reddish tinge. The liquid is seldom bloody. In many instances the organs of respiration are normal.

From two to three quarts of clear light yellow liquid are constantly found in the pericardium. This liquid is seldom bloody.

The heart, the liver and the kidneys look as if they had been cooked. The interior and exterior of the cardiac membrane often shew signs of bleeding.

The spleen is not swollen, but is of a dark bluish red.

The walls of the intestines are distended with water, the glands of the peritoneum are swollen. Effusion of blood may take place in the peritoneum and in all the serous and mucous membranes.

Horse Sickness then is a *true disease of the blood, death being brought on by the violent effect of poisonous matter upon the heart.* All the morbid changes that have been described are in the first place consequences of the weakening of the organs of circulation. In the Sickness, when artificially induced, it has been noticed that the most severe cases, and those in which death supervened most rapidly, often displayed only slight and scarcely visible symptoms.

The prediction in the case of horses brought into an infected district from one which is free from the disease, such as Argentina, is entirely unfavourable, leaving of course out of consideration the use of good stables and "sickness places".

Horses born of 'salted' parents have a fair prospect of recovering from the disease.

It is generally maintained that it makes a difference in what region the disease was acquired. Thus it is said to be more frequently the case that a horse recovers in the South of South West Africa than in the North of the Protectorate or beyond the River Cunene.

Mules and hinnies are doubtless better able to withstand the disease, in consequence of their descent from the ass, which is but little subject to it. I have had the same experience with inoculated cases.

In an advanced stage the Sickness is easy to recognize and can scarcely be mistaken, but at the beginning the diagnosis is very difficult. Frequently small swellings of the glands in the throat, cough owing to taking cold, fever from various causes, colic and other symptoms are taken for the beginning of the Sickness. The favourable passing away of these symptoms in a short time proves the suspicion to have been unfounded.

At the same time insignificant diseases of this kind have often caused horses to be indicated as immune, who have shortly afterwards fallen victims to the real horse-sickness.

The measures to be taken to provide against the disease have been mentioned above (page 6).

All kinds of treatment for the Sickness after it has broken out have been attempted. Quinine, a mixture of arsenic and sulphur, alcohol, common salt, etc. To quinine especially many farmers have ascribed a good effect, but I have myself found all these things of but little use. Opening a vein often does good service in combating the effusion of water in the lungs.

I have endeavoured to combat horse-sickness by means of Inoculation and have had the following experience.

Horse-sickness is always conveyed by inoculation with the blood of a sick or dying horse; ·005 ccm of blood is absolutely fatal. The fluids in the large cavities of the body will also produce the disease, but ·05 ccm is not always sufficient to do so. The specific poison is consequently present in these fluids in smaller quantity than in the blood. I may mention that the blood retains its efficacy for a year with the addition of 3 % of carbolic acid. An opportunit willy present itself below of speaking about the parasites found in the diseased blood.

I have discovered a serum against horse-sickness, which is able at the same time to heal the disease after it has broken out and also to bestow temporary immunity to a tolerably high degree. I postpone a more detailed account of the manipulation of the

serum. In the case of healthy animals no important reaction takes place even after injection of from 50 to 100 ccm of serum. The fever curves Nos 1, 2, 10, 11 and 14 belong to horses which were healed by injection of serum in the jugular vein.

By this serum I have saved some 50 per cent of the animals treated for horse-sickness naturally contracted, in spite of the fact that the horses were for the most part brought to me in an advanced stage of the disease.

To give immunity to healthy horses I have worked out several methods of applying the serum. The method which has given the best results up to the present time worked with a failure of 30 to 40 per cent. I hear, however, that in the recent severe epidemic of horse-sickness all the horses inoculated by this method in the Grootfontein District are still alive. Dr. Bail is at present assidnously engaged in pursuing these attempts in order to diminish the cases of failure more and more.

B. Malaria.

I now proceed to detail some of my own observations and to set forth the general views of modern times, so far as they are known.

The Chief Medical Officer of the Protectorate, Staff Surgeon Dr. Lübbert, assisted me with his advice and worked out with me the microscopic questions. Since the beginning of this year I have enjoyed the coöperation of Dr. Max Bail, who came over at my desire to settle in South West-Africa.

In regard to the history of Malaria as compared with other epidemic diseases I am inclined to believe that Malaria, like Cholera and Bubonic Plague, had its origin in a single locality. This locality lay apparently in The Old World. Thence the epidemic spread in earlier times over nearly the whole earth until it gradually became endemic everywhere.

The rinderpest is going through a similar process at the present time. In 1897 it raged for the first time in South West-Africa, it then disappeared, thanks to Koch's discovery of the efficacy of gall, and has been reappearing everywhere since 1900, though its spread has been rendered slow by the number of animals who were 'salted' at the former period.

Malaria has been introduced in South West-Africa by animals affected by the disease, coming from other countries.

Its spread in the Protectorate both in regard to place and time is readily explained on the hypothesis that the infection is conveyed by mosquitoes, for:

1. All places in South West-Africa which have no mosquitoes have also no endemic malaria. In many places of the south and on the coast, Europeans who are free from fever are able to settle without ever taking malaria.

2. No fresh cases of infection occur at the time when there are no mosquitoes. The mosquitoes die off in many places about May or June with the commencement of frost. They do not reappear till the beginning of the rainy season.

At the beginning of September 1896 about a hundred men of the Protectorate troops occupied a great part of the north, the districts of Outjo and Grootfontein. The first cases of malaria did not occur before the end of December, when the mosquitoes began to show themselves. No one was spared. I have as yet made no investigation as to the species of mosquito which carry the infection in South West-Africa.

The disease regarded purely from a clinical point of view displays as many different forms in S. W.-Africa as in all hot countries where it prevails. While the essential characteristic of the different forms of malaria is the marked alternation between the paroxysms and intervals of the fever, which has given rise to the name Intermittent Fever, the differences lie chiefly in the length of the intervals and of the attacks.

Thus the forms ordinarily observed are the Quotidian, Tertian, Quartan forms, recurring respectively: every day, every third*) day, every fourth day, and the Tropical form. Under this last name are understood in general those tertians in which the individual paroxysms last and display the small parasites for a longer time than the ordinary tertian. Of the way in which the different forms pass one into another I shall speak later.

We have now in my opinion to take into consideration the question whether the different symptomatic forms, which are all perhaps only varieties of the chief characteristic, do in reality indicate markedly distinct diseases. I have always held the view that malaria is in all cases one and the same disease.

It is even possible to hold the belief that the different forms belong to the essence of Intermittent-Fever and that the symptoms would not occur at all but for the sharply marked alternation between paroxysm and interval. I will speak more of this further on.

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*) This means the third day counting the day of a paroxysm as the first; thus if a paroxysm takes place on a Monday, the next in Tertian Ague would be on Wednesday, in Quartan on Thursday. — Trans.

The germs of the parasites of malaria come into the body with the sting of the mosquito, the saliva of the insect finding a place of least resistance at the point where the animal is stung. The development of the germs is promoted by a weak condition of the body. The first attack of fever breaks out as soon as a sufficient number of parasites are in circulation in the blood. This takes place after nine or ten days on an average. Before dying these parasites give rise to new germs, which however increase with far greater rapidity and give rise to the second attack. The longest interval is in the case of the quartan, and amounts to some seventy-two hours. The quartan, however, is very rare in South West Africa.

If the fever is not medically treated it continues for months as quotidian, tertian or quartan until the patient either dies or becomes "salted". The separate attacks get weaker and weaker and the disease imperceptibly disappears. This is the ordinary course with the fever of the natives.

Now there are doubtless cases, chiefly among Europeans, which become cured after a very large number of medically treated fevers. Then they display the condition which Ziemann*) calls Spontaneous Cure. Ziemann says "Under the term Spontaneous Cure is to be understood a case in which two or more attacks take place which gradually become weaker and finally disappear without quinine, recurring again after a shorter or longer time. A definitive cure without quinine is seldom or never attained."

In my opinion however permanent cure always takes place if the sick man will only have patience and not again have recourse to quinine.

The period from June 29th to July 26th 1897 was in many respects very instructive to me, as there was no quinine to be had in Grootfontein and there was no cessation in the attacks on the men. An epidemic of malaria of extraordinary violence had consumed all the supply in the country, while all goods traffic to the North was stopped for months by the rinderpest. The whole population of the district of Grootfontein had been attacked by fever often almost without interruption since January 1897. When quinine arrived again on the 26th of July the fever ceased as with a single blow. Of these people however, some fifteen in number, *not one was salted, all having been subject to fever for years after.*

I found myself at the time, with most of the men, in the region of the rinderpest.

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*) Ziemann. Über Malaria und andere Blutparasiten p. 71.

The few hospital assistants tended the people with devotion; iron and quinine, arsenic and methylene blue were given in some cases with success.

If no treatment had been available the fever would apparently have lasted for months longer, and as three people had already succumbed to weakness of the heart it is probable that many other deaths would have taken place. And from the condition in which I still found the people at the beginning of August — miserable, pale, emaciated and irritable, with swollen spleen and liver, weakened action of the heart, enfeebled digestion, one with even almost all the symptoms of Beri-beri — it is possible to form an idea of the chronic state into which the survivors had fallen.

In those localities of South West-Africa where there is much traffic and where there are many mosquitoes, all newborn children get malaria and either die of it or become 'salted' or immune. Infant mortality is therefore somewhat great. Districts enough however are to be found in which the natives grow up without taking the disease. As soon as they come into a malaria district at a later time they are attacked with the same violence as the whites. I have observed that immunity becomes weaker in the course of time and ceases entirely after from seven to ten years. As soon as immunity begins to give way the natives are again liable to take the disease.

According to my observations fresh infection of the natives often takes place under the appearances described by Ziemann as spontaneous cure, until the patient is again well "salted".

In the case of a life lasting for 70 years we might imagine from 7 to 10 attacks of the disease, unless indeed each seizure is followed by an increased period of immunity.

An enquiry among the natives themselves lasting only for a few months throws little light upon these questions; what is required is an observation of the same people for years together. This is a field which can only be worked by an experienced practitioner.

Among the symptoms of malaria in German South West-Africa I wish to emphasise that in addition to the organs of digestion the lungs are often attacked. In slight cases an attack of fever causes a feeble cough which comes and goes with the attack. Then there is to be heard in the lungs, especially during expiration, a laboured and sonorous breathing. In more severe cases there is usually a violent cough during the paroxysm, with all the symptoms of bronchitis or even inflammation of the lungs. Violent oppression and choking are also to be observed, which cease as soon as the paroxysm is over. In malaria of longer

duration the lung symptoms come so much into the foreground that the malaria proper is often no longer to be clinically recognized. Anyone who is observing carefully will take very frequent note of the pulmonary symptoms.

Finally we may recall the fact, that we have frequently observed in malaria the appearance, particularly in the month, of pustules, such as we are accustomed to regard as symptomatic of inflammation of the lungs.

Although I find that Ziemann has referred incidentally to the disease of the lungs, I communicate my own observations explicitly, because the frequency of these symptoms has recently been disputed more than once, and I should like to add a complete discussion of the question.

A second symptom which is very worthy of notice is often to be seen among the natives. This is a swelling of the skin, especially the skin of the head, which comes and goes with the paroxysm. These swellings often present the appearance of dropsy.

Thirdly, I should like to mention that I have seldom met with enlargement of the spleen in fresh cases of malaria.

About another question I should be glad of further information from my fellow practitioners. I have heard that according to the testimony of an English surgeon of the West Coast of Africa the blood of malaria patients does not lose its poisonous properties when carbolic acid is added to it. I myself have no experience in this matter.

Malaria is affected by a number of drugs. Besides quinine, methylene blue, arsenic, morphia, antipyrine and phenacetine are among the more efficacious. The native medicines, especially a root used by the Bushmen of South West Africa, are also of importance. It has however been so much the custom to look upon quinine as the only remedy that a cure without quinine is constantly called a spontaneous cure. I am of opinion that these spontaneous cures which do not follow a long series of paroxysms rest upon some other drug which has been taken. All such drugs suppress the attacks for a short time without actually curing the disease.

The influence of quinine upon malaria is marked and unfailing. Quinine is thus the specific *against* malaria.

But quinine also acts as a specific in the case of black-water fever, but it acts in favour of, and not against, this disease. In more than thirty cases of black-water which occurred in the district of Grootfontein in the years 1897, 1898 and 1899 there

*) p. 15 in the work cited above.

was only one in which no quinine had been taken shortly before the attack of black-water. I will not dispute the fact that there are other drugs which will give rise to black-water; thus I once observed a soldier just cured of black-water who had a relapse from taking beer. I can never lay the guilt upon alcohol, as my men had access to alcohol only very seldom in the course of the year. My position then is this: that *black-water fever in South West Africa is essentially due to quinine poisoning.*

It especially attacks those who have already been weakened by much fever and much taking of quinine. I have even made the observation that the faces of these people have a peculiar pale yellow colour. It was often very striking to me to see the transition from a blooming red to a pale reddish countenance with a distinct yellow tinge. *I have constantly treated black-water without quinine* and I found that the quinine which evoked the black-water was also sufficient to suppress the malaria.

These experiences induced me, in May 1898, to reduce the treatment of malaria from 30 grains of quinine to smaller and smaller doses. I saw however:

1. That 16 grains or even 8 grains easily give rise to black-water, leaving out of consideration the cases in which there was an oversensitiveness to quinine.

2. That this danger is reduced to a very slight one by giving from 1 to 2 grains at intervals ranging from half an hour to two hours.

3. That very often the whole amount of 8 grains was sufficient to relieve the fever. I am thus an advocate of the „drip-drop" administration of quinine. This word, as used in many books of instruction, acts like a sentence of excommunication on the young medical man and has already led to much black-water, to say nothing of other collateral effects of the quinine.

I have noticed besides that the quinine given during a fall of temperature is most efficacious when the pulse is just beginning to beat quietly and deliberately, more quietly in fact than in the patient's healthy days. I have consequently instructed my hospital assistants to determine the point of time for the administration of quinine by the pulse alone. This simple method suited the rude conditions of the colony, where it often happened that our last thermometer was broken.

When the attacks cease in consequence of the use of medicines, a longer time elapses until a return takes place. In spite of large doses of quinine with which the single paroxysm is treated,

the attacks recur with many people every eight or ten days. This recurrence is frequently brought on by mental emotion, sometimes only half an hour passing before the fever is again perceptible.

It may thus be maintained that the quinine ordinarily hinders the development of the germs but does not quite prevent it.

In order to keep off the return of the attacks, quinine must be used permanently. In 1897, following the suggestions of A. Pleyn, I introduced a mode of cure with quinine, in which 8 grains of quinine were given every six days. As I learned that this amount of quinine sometimes gave rise to black-water, I gave 4 grains at sunset and 4 at bedtime. I then noticed that this arrangement was much more effective than giving the 8 grains at once.

This quinine cure seldom failed me, the recurrences gradually ceased, while failing, nervous and sickly people recovered in a striking manner. I have not however observed that permanent immunity from malaria has ensued.

Accordingly I cast no doubt upon the observation of Koch, that making a place free from malaria is soonest attained by the systematic use of quinine. The condition is, that the population is completely secluded and accessible to the doctor. But the large quantity of quinine which Koch recommends does appear to me to be *objectionable on account of the black-water* and surprising when we remember Koch's publication on the subject of black-water.

A second method of extirpating malaria is getting rid of all standing water either by drainage or by filling up.

I have brought about the result by drainage works that places formerly notorious for fever, Grootfontein and Otavi, were almost entirely free from mosquitoes in the rainy season 1898/99. In doing this I learned that it is not the swamps which exist year after year, that chiefly produce mosquitoes, but what are called vleye. These are pools which are formed everywhere during the rainy season and hold water for a longish time, occasionally even to the next rainy season. Incredible masses of mosquitoes come from these vleye. When they lie in the vicinity of townships they are much more dangerous than the pools in the middle of the townships due to an overflow of the springs.

The permanent swamps, as is well known, have so much animal life which is hostile to the mosquitoes and their offspring that the development of these bloodsucking insects is much checked, while in rainwater tanks they flourish almost unmolested. In South West-Africa the vleye play the part of rainwater tanks.

Besides the means given above for combating malaria I have tried yet another, that of warding off the mosquitoes from people. I have had good results from this method on a small scale principally by the use of mosquito nets.

With very careful use of quinine, with drainage and with protection from mosquitoes, I succeeded in making Grootfontein almost entirely free from malaria in the year 1900. And thus, according to my idea, all the means recommended should be made use of simultaneously. It leads to nothing if each person recommends his own remedy and declares the others to be useless. Each remedy requires much trouble and labour and is therefore seldom completely carried out. But used together they promise to yield good results.

C. Relations between Malaria and Horse-Sickness in South West Africa.

As may be seen from the above remarks on malaria and horse-sickness, the two diseases have many points in common. It was already evident to me in the beginning of 1899 that there must be a very close connection between malaria and horse-sickness and I accepted it absolutely as a basis for my attempts in practice that I had to do with one and the same disease.

In consequence of this I used the curative serum of horse-sickness in the treatment of malaria.

I found, as we shall see, that the serum affected the malaria and indeed was able to cure it.

I will now place side by side the points of contact of the two diseases.

Horse-Sickness.	Malaria.
Not immediately infectious.	Ditto.
Appears with the rainy season and disappears with frost.	Fresh infections take place in the rainy season and cease with frost.
Only occurs where malaria prevails.	Prevails only in certain localities.
Crowded stables protect against horse-sickness.	Houses free from mosquitoes are a protection against malaria.
Infection by mosquitoes probable.	Infection by mosquitoes proved.
Is a pronounced disease of the blood.	Ditto.
Pulmonary disease is the chief symptom.	The lungs are often affected as well as the organs of digestion.
Swellings of the skin are almost always present.	Swellings of the skin, particularly in the face, do occur.

No enlargement of the spleen.	Enlargement of the spleen in fresh cases often not perceptible.
Transmission takes place with certainty by inoculation.	Ditto.
Three per cent of carbolic acid does not destroy the virus in the blood.	?
A serum has been found which 1. Gives temporary immunity 2. Cures horse-sickness that has broken out.	The serum of horse-sickness is also efficacious against malaria, as my cases will show.

I may remark that I do not bring forward the clinical resemblances as constantly present and as proof of my theory, but only because it is frequently maintained that the two diseases have clinically no points in common. A further relation will be noticed when I come to speak of inoculation for malaria.

In assuming absolutely that horse-sickness is the same disease as malaria I am quite conscious that it is a theory which still requires precise demonstration, and the question has to be raised whether the parasite is identical in the two cases, or whether there may not be an alternation of generation similar to that between the bladderworm and the tapeworm. Were this the case it would not be exactly correct to say that they are one and the same disease.

I have not yet made the attempt to transfer the disease from man to animal and vice versâ. This attempt will not succeed if an alternation of generations takes place in which the parasite has to go through development in some special host other than the mosquito, on the way from man to the horse. Thus Lübbert holds that some other widely spread living creature transfers the malarial poison.

The veterinary surgeon Rickmann, acting on my views, has made attempts to transfer the disease from man to horse, but he has not as yet been successful.

Now it has been objected that there are countries with a great deal of malaria, but without horse-sickness. On this point I should like to remark: Careful investigation will perhaps show that everywhere in tropical malarial countries horse-sickness either prevails or has only ceased to prevail owing to the gradual immunisation of the survivors. On the West Coast of Africa, for example, horses from the interior die suddenly, according to trustworthy information, with symptoms that much resemble those of horse-sickness. If, however, it were to be proved that there are tropical countries affected by malaria, in which there has never

been horse-sickness, we should be driven again to think of some special host. It is also quite possible that there is a particular species of anophele which conveys the horse-sickness.

The carriers of malarial poison have perhaps not yet been satisfactorily investigated. Neither the differences between the blood parasites found in numbers of animals and the parasite of malaria, nor unsuccessful attempts at transference by inoculation, nor indeed such isolated attempts at extirpating malaria as those made by Koch at Stephansort prove that there is no other living creature that can act as intermediary besides man and the mosquito. It is quite conceivable that in a systematic combating of human malaria, as for instance the quinine-cure, the malaria is extirpated in some place and yet that there is a third living creature concerned in which the parasites decrease step by step with the parasites of human malaria, and finally also disappear.

Zealous investigation has already been made as to the parasite of horse-sickness. The blood of such animals has been passed through a chamberland filter; Edington, and later Rickmann, have found that the filtrate is no longer capable of communicating the disease. Theiler and Mc. Faddan assert the opposite. These questions of filtration must be looked upon as not yet solved.

Edington formerly believed that he had discovered a fungus as the exciting cause of horse-sickness. Sander attributed it to the same cause as anthrax.

The first publication about parasites in the red corpuscles of the blood of affected animals which came under my view was an article by Dr. Carrington Purvis of Edinburgh, who, besides other micro organisms in the blood of animals suffering from horse sickness, describes the following parasites:

"A small spheric al body (like a coccus) inside of the red blood corpuscles. This coccus-like organism is somewhat difficult to find, and this for two reasons: 1st. it occurs sparingly in the blood, and 2nd. it is somewhat difficult to stain. I have, however, found it in every case of horse-sickness (some 3 or 4 cases) I have examined. In one specimen I found a ring-like form, not unlike the form figured in articles dealing with human malignant malaria, and in another specimen I occasionally found two coccus-like bodies inside a single red corpuscle, but this is rare. Till very recently I thought I was the first to note these spherical forms, but I am informed that one of the two Frenchmen who investigated rinderpest some three years ago in the Transvaal, (probably Bordet is meant), has found a spherical body inside some of the red corpuscles in horse sickness. I think that these intra-corpuscular parasites have something to do with horse-sickness.

Their constant presence (as far as I have observed) is, to say the least of it, most remarkable."

Rickmann somewhat later published a treatise on the bacilli of horse-sickness.*) The most important of his statements are the following: „From three to four days after inoculation, small points of a dark blue colour are found both within and without the red blood corpuscles. After a further day or two, besides these caryochromatophitous grains in the red corpuscles, a small round disc is found which has a distinctly blue tinge. The blue colour is for the most part complete, but in a few cases I have also observed that simply the peripheral zone was blue, the colour gradually diminishing towards the centre, the middle point itself showing no colour but a strong refracting power." Besides this, Rickmann, in blood drawn shortly before death, found forms partly corresponding to Apiosoma bigeminum and partly having the greatest similarity to the parasites of different forms of human malaria.

Then a paper has appeared quite recently on the parasites by Laveran. Laveran says somewhat as follows:

"In South Africa, especially in the Transvaal, a parasite is often found in the red corpuscles. It was first described by Bordet and Danysz at a conference in the Pasteur Institute in 1898. The preparations however were imperfectly coloured and did not permit of complete following up of the development. He received preparations of the blood and portions of the organs from Theiler, which he coloured by his own method. He describes the parasites as round forms resembling Piroplasma bigeminum and Piroplasma ovis and calls them Piroplasma equi. The smallest are $^1/_2\ \mu$, the largest $2^1/_2\ \mu$, the ordinary only $1—1^1/_2\ \mu$. They divide into 2 or 4 parts. The two parts always divide again, so that four new parasites are always produced.

The parasite is different from the Hæmamœba malariæ, especially in the simplicity of its shape, the manner of its propagation, its small size, the absence of pigment, and the absence of flagella. The observations which bring diseases of horses into relation with malaria, are not convincing. In Algiers no malaria has been observed in horses, although severe malaria prevails there. Inoculation of horses with malaria gives no result.

It is probable that some diseases of horses are dependent on Piroplasma equi, but the observations to hand are too incomplete.

"Horse-sickness" has nothing to do with Piroplasma equi; the two diseases frequently occur side by side.

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*) „Berliner Tierärztliche Wochenschrift" of July 5th 1900.

Nagana or Tsetse can no longer be brought into connection with malaria." — So far Laveran.

Unfortunately I have not been able to ascertain whether any publication of Bordet's is in existence. Laveran in his statements with regard to the occurrence of Piroplasma equi seems to rely on Theiler.

Theiler affirms 'that' up to the present time the latest methods of Bacteriology have not shewn any organism from sick animals which could have been brought into causative connexion with the disease". In this he apparently rests upon his experiments with the chamberland filter. He says nothing about Piroplasma equi. Perhaps he has piroplasma in his mind when he writes: "Malarial fever is also frequently confounded with horse-sickness." The pronounced saffron-yellow colour of the mucous membrane of the eye, the proof of plasmodia in the red corpuscles and the whole of the rest of the course of the disease, sufficiently distinguish Malarial fever.

The enquiries of Lübbert and myself have shewn that blood parasites are as easily proved to exist in horse-sickness as in malaria. They first make their appearence when the fever sets in.*) Their size has relation to that of the red corpuscles of the horse, as the size of the small malaria parasites to that of the red corpuscles of man. As the red corpuscles of the horse are smaller than those of man, so the parasites are smaller than those of malaria. At a certain stage of development they have the greatest resemblance to the small rings, especially under Ziemann's colouring. They are often strongly refractive.

We have seen figures of segments containing from two to six young parasites. We have also seen crescent shapes. Pigment was not to be distinctly seen in any case.

This is at the present moment the position of inquiries and opinions. I can at any rate say so much as this, that the occurrence of blood-parasites in horse-sickness does not militate against my theory.

D. The Results of Inoculation for Malaria.**)

I have tried the serum obtained in horse-sickness chiefly as a means of cure in fever after it had broken out. The inoculations began on the Emperor's birthday, Jan 27th 1899. In addition to

*) Deutsche Tierärztliche Wochenschrift 1901 No. 20. „Die südafrikanische Pferdesterbe".

**) Navy Surgeon Dr. Sander published a paper upon inoculation for malaria in the „Deutsche medizinische Wochenschrift." Nov. 1901, for which I beg here to express my best thanks.

numerous natives, about twenty white people had been inoculated by the beginning of April. In each case there was undoubted malaria. The examination of the blood confirmed the clinical diagnosis in most of the cases. Eleven fever curves of white people are recorded in the Table. (No. 4, 5, 6, 8, 9, 12, 13, 15, 16, 17, 18) During the treatment none of the patients took quinine.

For inoculation I employed one or more cubic centimetres of serum injected subcutaneously by a pravaz-syringe. I selected the fore-arm for the purpose. A small swelling resulted, which was painful for a few days and then disappeared leaving no mark. A nettle-rash often makes its appearance after several days, beginning with the inoculated arm and sometimes spreading over the whole body. The separate pimples itch a good deal, and are often very transitory. This symptom lasts only a few days. Otherwise no secondary symptoms have been observed as yet. Among healthy persons the injection even of several ccm has not been followed by any fever, pains in the limbs, or the like.

The effect on the course of the fever is perceptible in all forms of malaria, but is different in each individual case.

One thing is common to all cases, that the feeling of cold on the part of the patient diminishes with the attacks. The violent shivering of the tertian becomes simple coldness, then a mere chilliness in the legs, and finally all feeling of cold disappears. Secondly, the latest attacks are very lightly felt even when the temperature is tolerably high.

Now it is of the greatest importance whether the patient has already had much malaria or not. With the natives and old Africanders the inoculation often got rid of the attack at once. (See curves 6, 15, 17). Among whites who had recently come into the country and had never had malaria, and among children, four or five attacks on an average took place after the inoculation, the later attacks becoming weaker and weaker. (See Curves 5 and 12.) Between these two extremes lay the fevers of most of the white settlers who had already had malaria; among these from one to three attacks generally followed inoculation. (See Curves 4, 9, 13, 16, 18.)

A second point of importance is the kind of fever. In the case of the quotidian and tropic fever the return of the attacks is in general less frequent than in that of the tertian and quartan. The quartan is the most obstinate (see Curve 8).

Thirdly, it is to be noticed that the more serum is used the smaller is the number of attacks after inoculation.

Fourthly, the time of inoculation perhaps makes a difference, inoculation during a paroxysm being more effective than during an interval.

Now after the cessation of the attacks ensues an interval of for the most part three to four weeks. Then there is a return.

I shall call those attacks which occur immediately after inoculation Chief fevers, and the returns Subsidiary fevers. If in the case of a Tertian, Tropic, or Quartan, attacks occur during what should be intervals free from fever, I shall call them Intermediary attacks.

The duration of the Subsidiary fever varies, but is mostly from 5 to 7 days.

Its course is at times like other attacks of malaria, but more often it is quite different. In that case it produces a permanent sense of discomfort, with pains in the limbs generally, and great languor. The temperature seldom rises above 102° F. and is often quite inconsiderable. In Case 8 the temperature did not exceed 98.2° F. in spite of the fact that the patient both looked and felt very ill. The temperatures were as follows:

	20. 9. 99	21.	22.	23.
Morning	96,8	96.8	97,0	96,8
Noon	97,5	97,2	97,7	97,7
Evening	97.5	98.2	97,5	97,0

In Case No 12 the subsidiary fever followed immediately on the chief fever. We see here that it is no longer intermittent fever, but a permanent fever, the representation of which resembles that of a favourable case of horse-sickness (cf. Curves 1 and 11). The subsidiary fever disappears of itself without any medical treatment. The only requisite is complete rest; if the patient does not spare himself, higher temperatures and more violent symptoms may ensue.

There are often repetitions of subsidiary fevers.

We may here point out that in the subsidiary fevers we have proceedings which we may compare with the relapses in the case of horse-sickness, indicating again a close connexion between the two diseases.

It suffices for the explanation of the proceedings described, that we should pick out from the multitude of theories that have been put forward the following conclusions.

The parasites of infectious diseases cause degeneration of tissue. They draw nourishment from the body of the patient, work it up, secrete matter, and die. The results of degeneration are harmful to the parasites themselves as well as to the body.

The parasites are first roused by this matter to more lively activity, then made sluggish and finally killed, somewhat like an animal which sits in a confined space and is poisoned by the carbonic acid of its own breath. We may compare it with the fact that yeast when it has formed 14 per cent of alcohol, ceases to be active. The ammoniacal fermentation of urine by Micrococcus ureæ ceases when 13 per cent of carbonate of ammonia has been formed. The fermentation producing lactic acid by Bacterium acidi lactici ceases after ·8 per cent of lactic acid etc.

The body feels these materials as foreign substances, as poisons, and attempts to separate them, or at least to work them off and render them innocuous.

When these materials are more poisonous to the sick body than to the parasites, the body perishes. If they are more injurious to the parasites than to the cells of the body the former are destroyed in due time and the patient recovers. In this process many poisonous substances are excreted, but many are retained by the body and so changed as scarcely to operate as foreign bodies. Now these prevent new infection: from poisonous matters they have become protective matter, protecting the body against the parasites of the disease recovered from. They remain for years in the body, but disappear in the course of time.

If the protective matter of a disease is introduced into a healthy body without producing the disease itself, it remains for some time, at most some weeks, in the body.

We will now assume that materials have been introduced into the body by the inoculation we are considering, which are the same as, or very nearly related to, the protective matter of malaria.

While malaria ordinarily only forms a small quantity of protective matter at each attack, and only dies out slowly after a large number of attacks accompanied by danger to the life of the patient, the process is accelerated by inoculation, in consequence of the introduction of protective matter.

Now we have to consider the increase of the protective matter in connection with the quantity introduced, with the additional circumstance that by this increase the parasites of the malaria are roused to greater activity in forming matter.

The fever ceases when most of the germs are killed off and those which survive have no longer the strength to make themselves felt.

After some time, generally three or four weeks (see above), the protective material which has been introduced into the body from without has been again completely excreted. Now the

parasites remaining in the tissues of the body have the opportunity of germinating once more. Their freedom however is a limited one, as the protective material formed in the first fever is permanently incorporated in the body. This protective material combats the parasites of the subsidiary fever which ceases so soon as all the parasites, or at least the great mass of them, are destroyed.

In case the few survivors get a new opportunity of germinating, as when perhaps the equilibrium of the body suffers some special disturbance from mental excitement or debauchery, this generation destroys itself through its own matter in the second subsidiary fever. Now if the formation of protective matter has not been plentiful enough to give the subsidiary fever the character of intermittent fever, it corresponds exactly to the fever described by Ziemann as incident to spontaneous cure. So soon as the protective matter is present in sufficient abundance the subsidiary fever assumes the character described above, in which the rise of temperature is small and the discomfort very pronounced. This kind of subsidiary fever leads to a permanent cure.

This statement also supplies the explanation of the fact mentioned above, that the earlier fevers have to be taken into consideration in regard to inoculation. Every fever, even when it has been checked by quinine, forms some protective matter, if only a little. It is thus quite natural that earlier fevers have less influence than later ones, as the protective matter disappears in the course of time.

That the kind of fever is of much importance is explained in the following way by the theory now advanced.

The property of the malaria parasites, that they form only a small quantity of protective matter at each attack, carries with it the further property that the parasites, if uninjured by their protective matter, are able to carry out regular development in quiet.

The parasites of the quartan have the longest periods of rest, they form the least amount of protective matter. In the case of quartan fever from Grootfontein which we have represented in curve 8, the fever set in regularly every 4 days*) shortly before 4 o'clock in the afternoon. Each attack commenced with a somewhat violent fit of shivering, which was soon replaced by heat, there was scarcely any perspiration. The disease had no specially troublesome secondary symptoms, such as headache or nausea. By seven or eight o'clock in the evening the attack had passed, but the temperature only became quite normal during the night. On

*) Really this should be every three days, as we should count it in England. Trans.

he two following days the patient felt quite well. It was only a few minutes before the attack that he became sensible that the fever was again rising. The alternation was wonderfully regular. I performed inoculation first during one of the feverless intervals, but perceived no result. Then I determined to inoculate during the attack (13th, 16th, 19th of July 1899). In the next attack the symptoms of illness were already small. In the attack on the 22nd the shivering fit was slight. On the 23rd and 24th, the days following the attack, followed marked indisposition, which rose on the 26th and 27th to regular fever without shivering but with violent pains and nausea. The attacks of the 25th, 28th and 31st were accompanied by only a slight feeling of cold and no longer any shivering. The attack on the 31st did not commence until evening and was then accompanied with violent pains in the limbs. The attacks on the 3rd, 6th and 9th of August set in later and later in the evening and were unaccompanied with the sensation of cold. On the 3rd there were still pains in the limbs, on the 6th and 9th there were scarcely any symptoms except elevation of temperature. The intermediary attacks lasted until the 2nd of August and there were violent pains in the limbs on the 27th and 29th of July and on the 1st of August.

The last attack of chief fever was on the 9th of August. Subsidiary fever shewed itself on the 19th of September and lasted some days.

I was thus able to observe accurately how the formation of protective matter made itself noticeable in the pains of the limbs generally, how it led to the intermediary attacks, and ended the disease with the subsidiary fever.

It is quite out of the question that the intermediary attacks should have been due to new infection, as there were at that time no cases of infection in Grootfontein.

The great majority of the parasites stopped their original course of development; many, however, increased too early in consequence of the incitement of the matter, and gave rise first to indisposition and then to fever according to their quantity. Thus there was a quotidian from the 23rd of July to the 3rd of August, which was evoked not by three different quartans but by a single one.

The parasites of the tertian form more protective matter than those of the quartan, and are therefore also sooner excited to reappear. The parasites of the quotidian and still more of the tropic form a still greater quantity of protective matter. Now if these forms are put under the influence of inoculation, the attacks cease sooner than in the case of the quartan, and we

may say that in general the numbers of the attacks increase in the following order: Tropic, Quotidian, Tertian, Quartan.

Distinct attacks of an intermediary character such as those in the case of the quartan described above, are not observed after inoculation in the case of the other forms, but the regularity of the attacks frequently ceases. In the subsidiary attacks, in which the formation of protective matter is often very pronounced, there is no longer any trace of regular intermittent fever. (Cf. cases 8 and 12.) It is of course quite clear that even without inoculation cases of malaria are observed which, like these subsidiary fevers, in consequence of the operation of protective matter produce not intermittent but continuous fever. What is called spontaneous cure presents at its close the same picture if the attacks are not medically treated.

In the case of the horse the parasites similarly take the field with such a formation of matter, that continuous fever and a violently fatal disease follows. Many heavy cases of tropic fever also display an uncommonly profuse development of matter.

The fact that the development in the case of the South African horse is different from that in the case of man gives rise to the suspicion, that man and the horse offer different soil for the nourishment of malaria. The differences again in the different forms affecting man are apparently due to differences in external influences. The question whether a population has had malaria since ancient times is certainly one of importance. Climate and season of the year appear also to play an important part, the tropic form increasing in S. W. Africa towards the hotter and damper north.

Now I assert that under these influences, when they have been continually at work for a long time on the malaria, the quartan, tertian, etc. forms are produced as in a certain sense "varieties", and the parasites of these forms have a tendency to preserve their course of development even after transmission to other people.

In the whole of this discussion I have not entered upon the question through what parasite the quotidian arises. As I see only varieties in all forms of malaria parasite, I believe it may very well be that quotidian can be evoked by species already generated, as Marchiafava and Bignami, two of the most eminent investigators of malaria, maintain. The beginning of this breeding then is a quotidian, which is temporarily evoked by the too early maturing of quartan or tertian parasites of one species, as has been explained above in Case 8.

I also explain to myself the appearance of Quartana duplicata by the proceedings in the formation of matter.

It appears however very improbable to me that tertian or quartan species completely independent of one another should produce the attacks alternately, as one sentinel relieves another. It is indeed credible that a species of parasite which comes by new infection in addition to what is there already, will make use of the time when the body is weakened by the attacks.

Thirdly that the quantity of serum used is of importance is now clear without further discussion. In this connection it may very well be that perhaps by a too large application of serum the whole of the parasites might be destroyed, so that there would be no subsidiary fever at all. Then after a few weeks the protective matter introduced would disappear and the permanent protective matter remaining would at the end be only small.

A new infection could then doubtless take place.

Lastly the time at which inoculation is performed is so far of importance that in inoculating at the time of a paroxysm the parasites in the act of growing will be affected by the whole mass of the introduced protective matter and incited to formation of matter, while in inoculating in the interval the body has already altered or excreted the introduced protective matter when the paroxysm takes place.

The substances found in the blood in cases treated by inoculation will be discussed in a special work.

The result of inoculation may be measured from the present considerations.

There are three results to be aimed at: —

1. Relief of the actually existing paroxysm, a substitute for quinine.

2. Destruction of all parasites in the blood and avoidance of relapses.

3. Protection against fresh infection.

In many cases inoculation has relieved the actual fever without being followed by further attacks. If this goal can be attained in all cases by injection of more serum, then a substitute for quinine would be gained which would avoid the disadvantageous collateral effects, especially the danger of black-water fever. In that case Result No. 1 would be attained.

Unfortunately, owing to the vicissitudes and undeveloped condition of the colony, it was not possible for me to make a continuous and accurate observation of all who were inoculated. Thus I have only been able in two cases to obtain records of the temperature of the subsidiary fever fit for publication (see

above and curve 12). For over three years I was District Superintendent of Grootfontein and in this position was obliged to make many journeys under the roughest conditions. I had often to leave important observations to my subordinates.

Still I am able to state that even of the cases inoculated in 1899 and 1900, in which the operation of the subsidiary fever had not been interfered with by quinine, no further fever shewed itself after the cessation of the subsidiary fevers until the beginning of March, 1901. In the case of the whites a second subsidiary fever occurred in three instances, and in two instances there was a third as well. In one case the patient says that he had no subsidiary fever. But even here no new fever has as yet followed.

This seems to shew that Result No. 2 may have been attained.

One view of this that may be taken, as we have seen, is that by inoculation during the chief fever all germs are killed off. Perhaps this was the case with No. 18. Although I should like to maintain, even in this case, that there had been a subsidiary fever of quite a slight character.

The other view is that some germs do remain. These germs are then brought to development by some derangement of the equilibrium of the body and evoke subsidiary fevers from time to time until they are finally eradicated.

If however it is maintained that on the one side the body remains without disturbance for a longish time after the chief fever or after a subsidiary fever, and on the other side that the number and the strength of the remaining parasites are very small, then the parasites perhaps first break out again later when the protective matter formed by them has already disappeared. No. 18 might be a case of this kind in the end.

Thus some light has been thrown on the question of Result No. 3.

Either the inoculation in the chief fever quickly gets rid of all the parasites before sufficient protective material has been formed, and then it is after a time no longer a protection against fresh infection,

Or else, in the killing off of all parasites, sufficient protective matter has been formed, and in that case there would be immunity lasting for a longer time. The same happens if germs are left behind, and are then destroyed by the subsidiary fever.

As we see from this discussion, much depends on the manner of inoculation, especially the amount of serum used and the time of operating. Further it has to be examined what result follows if the subsidiary fever is again treated by inoculation.

In general it is not yet decided whether Results No. 2 and No. 3 are to be disputed. Koch endeavours to attain result No. 2, especially in the case of children, by his quinine-cure. In this we give up the advantage of the natural immunisation of the patient. This is only justified, as F. Plehn forcibly sets forth out of his great experience in the February number of this year's "Archivs", if a real extirpation of malaria is possible by means of quinine. This seems to be impossible for many regions of the earth. Whether it will be possible to introduce inoculation in these places the future will shew.

In order to make successful use of this inoculation in other countries than South West-Africa two conditions must be fulfillled:

First, it must be possible to send the serum to other countries in an effective state. Within South West-Africa I have sent the serum to a distance, and kept it a long time, without its losing its efficacy.

Secondly, malaria must be really, as I maintain that it is, the same everywhere as in South West-Africa.

So soon as I am quite clear upon these questions, and so soon as this inoculation shall have been yet further tried and established in practice, I propose to make the serum accessible to general use.

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